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Theory of Granulation

Larry L. Augsburger and Murali K. Vuppala
University of Maryland at Baltimore, Baltimore, Maryland

I. INTRODUCTION

A. Definition of Granulation

Granulation may be considered a size-enlargement process during which small particles are formed into larger, physically strong agglomerates in which the original particles can still be identified. In modern times, granulation technology has been used by a wide range of industries, ranging from

Table 1 The Advantages and Disadvantages of Wet Granulation

Advantages	Disadvantages
Improved flow properties	Multiple processing steps add complexity and make validation and control difficult
Densification	Time, space, and equipment required are costly
Improved compression characteristics	Stability may be a concern for moisture-sensitive or thermolabile drugs
Better distribution of color and soluble drugs if added in binder solution	Loss of material during various stages of processing
Reduction in dusting	
Prevention of segregation of powder mix	
Makes hydrophobic surfaces more hydrophilic	

the pharmaceutical industry to the fertilizer and minerals-processing industries. Even though pharmaceutical granulations are used primarily to prepare materials for tableting, some granulations are dispensed as such in packets or capsules.[7]

The main objectives of granulation are to improve the flow properties and compression characteristics of the mix, and to prevent segregation of the constituents. However, these gains must be weighed against the fact that granulation requires multiple unit processes, such as wet massing, drying, and screening, which are costly in terms of the time, space, and equipment required, and add complexity because each unit process brings its own set of complications. The advantages and disadvantages of wet granulation are summarized in Table 1.

B. Types of Granulation

The principal methods of granulating pharmaceuticals may be classified into three main categories: wet processes, dry processes, and other processes. In the wet granulation process, a granulating liquid is used to facilitate the agglomeration process. In the dry granulation process, dry powder particles may be brought together mechanically by compression into slugs or, more frequently today, by roller compaction. Table 2 subdivides each of these

Table 2 Processes Used for Pharmaceutical Granulations

General process	Specific methodology
Wet processes	Wet massing
	Fluid bed granulation
	Spray drying
	Pan granulation
	Extrusion and pelletizing
Dry processes	Roller compaction
	Slugging
Other processes	Humidification
	Prilling
	Melt pelletization

Source: Ref. 1.

categories into specific methods of preparation as given by Record [1]. Although some or all these methods are used in the pharmaceutical industry, wet granulation has been, and continues to be, the most widely used agglomeration process. Typically, the wet massing of pharmaceutical powders is carried out in high-shear mixers before wet screening, and often, the moist granules are dried in fluidized bed equipment. Often, wet granulation is also carried out in fluid bed drier–granulators in which the liquid phase is sprayed onto fluidized powders as the hot airflow simultaneously dries the granules. This latter process requires fewer handling steps and reduces the time and space needed for granulation. Moreover, it can be readily automated. Other processes are used less frequently.

II. MECHANISMS OF PARTICLE BONDING

To understand the mechanism of granulation, it is useful to consider the forces giving rise to the cohesion of moist particles and to the phenomena of adhesion and cohesion. *Adhesion* may be defined as the bonding of unlike materials, whereas *cohesion* is that of like materials. Pharmaceutical dosage forms are heterogeneous and contain powders of varying physical properties. Bonds must be formed between powder particles so that they adhere together to form granules, and these bonds must be sufficiently strong to prevent breakdown of the final dried granules to powder in subsequent handling operations. The magnitude of these forces is determined by the size of the particles, the structure of the granule, the moisture content, and the surface tension of the liquid.